Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the specification:

Listing of Claims

1. A method to treat, prevent or ameliorate pathological conditions associated with Aβ secretion comprising administering to a subject in need thereof an effective amount of one or more modulators of one or more proteins selected from the group consisting of those disclosed in Table 1.

2. The method of claim 1 wherein said proteins are selected from the group consisting of cyclophilin F, carboxypeptidase Z, Calmodulin 2, TOB3, TLL2, protease E, chymotrypsinogen B1, Bone morphorgenic protein BMP45 (BMP45), ANG2 gene, type 1 tumor necrosis factor receptor shedding aminopeptidase regulator (ARTS-1), Fas (TNFRSF6)-associated via death domain (FADD), mitogen-activated protein kinase 4 (MAPK4), N-acylsphingosine amidohydrolase (acid ceramidase) and tryptase beta.

3. The method of claim 1 ~~or 2~~ wherein said modulator inhibits activity of said protein in said subject.

4. The method of claim 1 ~~or 2~~ wherein said modulator inhibits gene expression of said protein in said subject.

5. The method of claim 1 ~~or 2~~ wherein said modulator comprises any one or more substances selected from the group consisting of antisense oligonucleotides, triple helix DNA, ribozymes, RNA aptamers, siRNA and double or single stranded RNA wherein said substances are designed to inhibit gene expression of said protein.

6. The method of claim 1 ~~or 2~~ wherein said modulator comprises one or more antibodies to said protein, or fragments thereof, wherein said antibodies or fragments thereof can inhibit activity of said protein.

7. The method of claim 1 ~~or 2~~ wherein said pathological conditions are selected from the group consisting of Alzheimer's Disease, Parkinson's Disease, tauopathies, prion diseases, frontotemporal dementia, striatonigral degeneration, Lewd body dementia, Huntington's disease, Pick's disease, amyloidosis, and other neurodegenerative disorders associated with excess Aβ production.

8. A method to treat, prevent or ameliorate pathological conditions associated with Aβ secretion comprising administering to a subject in need thereof a pharmaceutical composition comprising an effective amount of one or more modulators of any one or more proteins selected from the group consisting of those disclosed in Table 1.

9. The method of claim 8 wherein said proteins are selected from the group consisting of cyclophilin F, carboxypeptidase Z, Calmodulin 2, TOB3, TLL2, protease E, chymotrypsinogen B1, Bone morphorgenic protein BMP45 (BMP45), ANG2 gene, type 1 tumor necrosis factor receptor shedding aminopeptidase regulator (ARTS-1), Fas (TNFRSF6)-associated via death domain (FADD), mitogen-activated protein kinase 4 (MAPK4), N-acylsphingosine amidohydrolase (acid ceramidase)and tryptase beta.

10. The method of claim ~~8 or 9~~ wherein said modulator inhibits activity of said protein in said subject.

11. The method of claim ~~8 or 9~~ wherein said modulator inhibits gene expression of said protein in said subject.

12. The method of claim ~~8 or 9~~ wherein said modulator comprises any one or more substances selected from the group consisting of antisense oligonucleotides, triple helix DNA, ribozymes, RNA aptamers, si RNA and double or single stranded RNA wherein said substances are designed to inhibit gene expression of said protein.

13. The method of claim ~~8 or 9~~ wherein said modulator comprises one or more antibodies to said protein, or fragments thereof, wherein said antibodies or fragments thereof can inhibit activity of said protein.

14. The method of claim ~~8 or 9~~ wherein said pathological conditions are selected from the group consisting of Alzheimer's Disease, Parkinson's Disease, tauopathies, prion diseases, frontotemporal dementia, striatonigral degeneration, Lewd body dementia, Huntington's disease, Pick's disease, amyloidosis, and other neurodegenerative disorders associated with excess Aβ production.

15. A method to identify modulators useful to treat, prevent or ameliorate pathological conditions associated with Aβ secretion comprising assaying for the ability of a candidate modulator to inhibit the activity of a protein selected from the group consisting of those disclosed in Table 1.

16. The method of claim 15 wherein said proteins are selected from the group consisting of cyclophilin F, carboxypeptidase Z, Calmodulin 2, TOB3, TLL2, protease E, chymotrypsinogen B1, Bone morphorgenic protein BMP45 (BMP45), ANG2 gene, type 1 tumor necrosis factor receptor shedding aminopeptidase regulator (ARTS-1), Fas (TNFRSF6)-associated via death domain (FADD), mitogen-activated protein kinase 4 (MAPK4), N-acylsphingosine amidohydrolase (acid ceramidase)and tryptase beta.

17. The method of claim 15 ~~or 16~~ wherein said method further comprises assaying for the ability of an identified inhibitory modulator to reverse the pathological effects observed in any one or more animal models of said pathological conditions.

18. The method of claim 15 ~~or 16~~ wherein said method further comprises assaying for the ability of an identified inhibitory modulator to reverse the pathological effects observed in clinical studies with subjects with said pathological conditions.

19. The method of claim 15 ~~or 16~~ wherein said pathological conditions are selected from the group consisting Alzheimer's Disease, Parkinson's Disease, tauopathies, prion diseases, frontotemporal dementia, striatonigral degeneration, Lewd body dementia, Huntington's disease, Pick's disease, amyloidosis, and other neurodegenerative disorders associated with excess Aβ production.

20. A method to identify modulators useful to treat, prevent or ameliorate pathological conditions associated with Aβ secretion comprising assaying for the ability of a candidate modulator to inhibit gene expression of a protein selected from the group consisting of those disclosed on Table 1.

21. The method of claim 20 wherein said proteins are selected from the group consisting of cyclophilin F, carboxypeptidase Z, Calmodulin 2, TOB3, TLL2, protease E, chymotrypsinogen B1, Bone morphorgenic protein BMP45 (BMP45), ANG2 gene, type 1 tumor necrosis factor receptor shedding aminopeptidase regulator (ARTS-1), Fas (TNFRSF6)-associated via death domain (FADD), mitogen-activated protein kinase 4 (MAPK4), N-acylsphingosine amidohydrolase (acid ceramidase) and tryptase beta.

22. The method according to claim 20 ~~or 21~~ wherein said method further comprises assaying for the ability of an identified inhibitory modulator to reverse the pathological effects observed in any one or more animal models of said pathological conditions.

23. The method according to claim 20 ~~or 21~~ wherein said method further comprises assaying for the ability of an identified inhibitory modulator to reverse the pathological effects observed in clinical studies with subjects with said pathological conditions.

24. The method of claim 20 ~~or 21~~ wherein said pathological conditions are selected from the group consisting of Alzheimer's Disease, Parkinson's Disease, tauopathies, prion diseases, frontotemporal dementia, striatonigral degeneration, Lewd body dementia, Huntington's disease, Pick's disease, amyloidosis, and other neurodegenerative disorders associated with excess Aβ production.

25. A pharmaceutical composition comprising one or more modulators of any one or more proteins selected from the group consisting of those disclosed in Table 1 in an amount effective to treat or ameliorate pathological conditions associated with Aβ secretion in a subject in need thereof.

26. The pharmaceutical composition according to claim 25 wherein said proteins are selected from the group consisting of cyclophilin F, carboxypeptidase Z, Calmodulin 2, TOB3, TLL2, protease E, chymotrypsinogen B1, Bone morphorgenic protein BMP45 (BMP45), ANG2 gene, type 1 tumor necrosis factor receptor shedding aminopeptidase regulator (ARTS-1), Fas (TNFRSF6)-associated via death domain (FADD), mitogen-activated protein kinase 4 (MAPK4), N-acylsphingosine amidohydrolase (acid ceramidase) and tryptase beta.

27. The pharmaceutical composition according to claim 25 ~~or 26~~ wherein said pathological conditions are selected from the group consisting of Alzheimer's Disease, Parkinson's Disease, tauopathies, prion diseases, frontotemporal dementia, striatonigral degeneration, Lewd body dementia, Huntington's disease, Pick's disease, amyloidosis, and other neurodegenerative disorders associated with excess Aβ production.

28. The pharmaceutical composition according to claim 25 ~~or 26~~ wherein said modulator inhibits the activity of said protein.

29. The pharmaceutical composition according to claim 25 ~~or 26~~ wherein said modulator inhibits gene expression of said protein.

30. The pharmaceutical composition of claim 25 ~~or 26~~ wherein said modulator comprises any one or more substances selected from the group consisting of antisense oligonucleotides, triple helix DNA, ribozymes, RNA aptamer, siRNA and double or single stranded RNA wherein said substances are designed to inhibit gene expression of said protein.

31. The pharmaceutical composition of claim 25 ~~or 26~~ wherein said modulator comprises one or more antibodies to said protein, or fragments thereof, wherein said antibodies or fragments thereof can inhibit activity of said protein.

32. A method to diagnose subjects suffering from pathological conditions associated with Aβ secretion who may be suitable candidates for treatment with one or more modulators of any one or more proteins selected from the group consisting of those disclosed in Table 1 comprising assaying mRNA levels of said protein in a biological sample from said subject wherein a subject with increased mRNA levels compared to controls would be a suitable candidate for modulator treatment.

33. The method of claim 32 wherein said proteins are selected from the group consisting cyclophilin F, carboxypeptidase Z, Calmodulin 2, TOB3, TLL2, protease E, chymotrypsinogen B1, Bone morphorgenic protein BMP45 (BMP45), ANG2 gene, type 1 tumor necrosis factor receptor shedding aminopeptidase regulator (ARTS-1), Fas (TNFRSF6)-associated via death domain (FADD), mitogen-activated protein kinase 4 (MAPK4), N-acylsphingosine amidohydrolase (acid ceramidase) and tryptase beta.

34. A method to treat, prevent or ameliorate pathological conditions associated with Aβ secretion comprising

    (a) assaying a subject for mRNA levels for any one or more proteins selected from the group consisting of those disclosed in Table 1; and,

    (b) administering to a subject with increased levels of mRNA compared to controls a modulator of any one or more of said proteins in an amount sufficient to treat or ameliorate said pathological conditions.

35. The method of claim 34 wherein said proteins are selected from the group consisting of cyclophilin F, carboxypeptidase Z, Calmodulin 2, TOB3, TLL2, protease E, chymotrypsinogen B1, Bone morphorgenic protein BMP45 (BMP45), ANG2 gene, type 1 tumor necrosis factor receptor shedding aminopeptidase regulator (ARTS-1), Fas (TNFRSF6)-associated via death domain (FADD), mitogen-activated protein kinase 4 (MAPK4), N-acylsphingosine amidohydrolase (acid ceramidase)and tryptase beta.

36. The method of claim 33 ~~or 34~~ wherein said pathological conditions are selected from the group consisting of Alzheimer's Disease, Parkinson's Disease, tauopathies, prion diseases, frontotemporal dementia, striatonigral degeneration, Lewd body dementia, Huntington's

disease, Pick's disease, amyloidosis, and other neurodegenerative disorders associated with excess Aβ production.

37. A method to treat, prevent or ameliorate pathological conditions associated with Aβ secretion comprising:

    (a) assaying a subject for protein levels of any one or more proteins selected from the group consisting of those disclosed in Table 1; and,

    (b) administering to a subject with increased protein levels compared to controls a modulator of any one or more of said proteins in an amount sufficient to treat or ameliorate said pathological conditions.

38. The method of claim 37 wherein said proteins are selected from the group consisting of cyclophilin F, carboxypeptidase Z, Calmodulin 2, TOB3, TLL2, protease E, chymotrypsinogen B1, Bone morphorgenic protein BMP45 (BMP45), ANG2 gene, type 1 tumor necrosis factor receptor shedding aminopeptidase regulator (ARTS-1), Fas (TNFRSF6)-associated via death domain (FADD), mitogen-activated protein kinase 4 (MAPK4), N-acylsphingosine amidohydrolase (acid ceramidase)and tryptase beta.

39. The method of claim 37 ~~or 38~~ wherein said pathological conditions are selected from the group consisting of Alzheimer's Disease, Parkinson's Disease, tauopathies, prion diseases, frontotemporal dementia, striatonigral degeneration, Lewd body dementia, Huntington's disease, Pick's disease, amyloidosis, and other neurodegenerative disorders associated with excess Aβ production.

40. A diagnostic kit for detecting mRNA levels or protein levels of a protein selected from the group consisting of those disclosed in Table 1 in a biological sample, said kit comprising:

    (a) a polynucleotide of said protein or a fragment thereof;

    (b) a nucleotide sequence complementary to that of (a);

    (c) an RNAi sequence complementary to that of (a);

    (d) said protein, or a fragment thereof; or

    (e) an antibody to said protein wherein components (a), (b), (c),(d) or (e) may comprise a substantial component.